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In re Application of : Decision on Petition  
Kock et al :  
Serial No. : 09/701,586 :  
Filed : 30 November 2000 :  
Attorney Docket No. : 49790 :

This letter is in response to the Petition for Reconsideration of Restriction Requirement under 37 C.F.R. 1.144 filed on August 04, 2003. The delay in acting upon this petition is regretted.

**BACKGROUND**

This application is filed as 35 USC 371 of the National Stage filing of PCT/EP99/03889, filed 04 June 1999.

A review of the file history shows that on 24 September 2002, the Examiner instituted a lack of unity requirement of claims 1-32 into fifteen groups. Further the Examiner selected a certain motifs and made an additional Restriction Requirement solely among the sequences directed towards SEQ ID Nos: 1-13 and 15-19. Examiner has cited Lepiniec et al (FEBS 364: 103-108, 1995) to show that the claimed inventions lack unity.

Applicants filed a response to the lack of unity along with amendments to claims on 25 October 2002. Applicants elected group I and selected the invention of SEQ ID NO:2 with traverse.

On 13 January 2003, the Examiner in the Non-final Office Action addressed the Applicants traversal of election of group I, and selected invention of SEQ ID NO: 2, stated that the selection of SEQ ID NO: 2 is considered as restriction and is not election of species and made the Restriction Requirement Final.

Applicants filed a response (including Affidavits) to the Non-final office Action and amendments to claims on 08 July 2003.

A Petition for Reconsideration of Restriction Requirement was filed on August 04 2003.

On 26 September 2003, a Final office Action was filed in this application.

Applicants filed amendments to the claims and a Request for Continued Examination of this application on 01 March 2004.

In the Petition filed on 04 August 2003, the unity of invention between groups I-XV in general and particularly between group I and groups V-VI is at issue.

Group I, original claims 1-4, drawn to poly (ADP-ribose) polymerase (PARP) homolog containing NAD<sup>+</sup> binding domain but without zinc finger sequence motif of the general formula (SEQ ID NO: 30).

Group II, original claim 5, drawn to a binding partner for PARP homologs, which is an antibody.

Group III, original claim 5, drawn to a binding partner for PARP homologs, which is a protein-like compound.

Group IV, original claim 5, drawn to a binding partner for PARP homologs, which is a low-molecular weight effector, and method of using the PARP binding partners for the diagnosis of pathological states.

Group V, original claims 6-10, drawn to a nucleic acid encoding at least one PARP homolog, an expression cassette, a recombinant vector, and recombinant microorganism comprising at least one recombinant vector.

Group VI, original claim 11, drawn to a transgenic mammal comprising at least one recombinant vector.

Group VII, original claim 12, drawn to a PARP deficient eukaryotic cell or a PRP-deficient mammal.

Group VIII, original claims 13-22, drawn to a method of in-vitro detection for PARP inhibitor using PARP homolog.

Group IX, original claim 23, drawn to a method for in-vitro screening binding partners for a PARP homolog.

Group X, original claims 24, 27, drawn to a method for the qualitative or quantitative determination of nucleic acids encoding PARP homolog.

Group XI, original claims 25-26, drawn to method of qualitative or quantitative determination of encoding PARP homolog.

Group XII, original claim 28, drawn to a method for determining the efficacy pf PARP effectors.

Group XIII, original claim 29, drawn to a gene therapy composition comprising an antisense nucleic acid against a coding nucleic acid, which encodes PARP homolog.

Group XIV, original claim 30, drawn to a pharmaceutical composition comprising PARP protein.

Group XV, original claims 31-32, drawn to a method of using low-molecular weight PARP binding partners for therapy.

## **RELEVANT AUTHORITY**

An international or a national stage application are considered to have unity of invention where there exists a “special technical feature” that defines a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. See PCT Rule 13.2; 37 CFR 1.475(a), (b)(1) and(2).

In addition to the categories provided for in 37 CF 1.475(b) (1-5), unity of invention is provided for in the following context:

Claim 1: Protein X

Claim 2: DNA sequence encoding protein X.

wherein expression of the DNA sequence in a host results in the production of a protein, which is determined by the DNA sequence. The protein and the DNA sequence exhibit corresponding special technical features. Unity of invention between claims 1 and 2 is accepted.

See MPEP 1893.03(d) and Annex B, Part 2 of the PCT Administration Instructions, Example 17.

Unity of invention has to be considered in the first place only in relation to the independent claims in an international and not the dependent claims and (i) If the independent claims avoid the prior art and satisfy the requirement of unity of invention, no problem of lack of unity arises in respect of any claims that depend on the independent claims; (ii) If however, an independent claim does not avoid the prior art, then the question whether there is still an inventive link between all the claims dependent on the claim need to be carefully considered. If there is no link remaining an objection of lack of unity a posteriori (that is, arising only after assessment of the prior art) may be raised. See ANNEX B: Unity of Invention Part 1 “Instructions Concerning Unity of Invention” MPEP AI-6 (Rev. 1. Feb. 2003).

According to PCT Rule 13.2 and to the guidelines in Section (f) of Annex B of the PCT Administrative Instructions, the situation involving the so-called “Markush practice” wherein a single claim defines alternatives (chemical or non-chemical), the requirement of a technical

interrelationship and the same or corresponding special technical features as defined in Rule 13.2, shall be considered to be met when the alternatives are of a similar nature.

(i) When the Markush grouping is for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:

(A) all alternatives have a common property or activity, and

(B) (1) a common structure is present, i.e., a significant structural element is shared by all of the alternatives, or

(B) (2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

(ii) In paragraph (f)(i)(B)(1), above, the words "significant structural element is shared by all of the alternatives" refer to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common only a small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of existing prior art. The structural element may be a single component or a combination of individual components linked together.

## DISCUSSION

The petition and application file history have been considered carefully.

The above-identified application is a national stage application submitted under 35 U.S.C. 371 to which "unity of invention", and not U.S. restriction practice is applicable. MPEP section 189.03(d). The lack of unity between the groups I, and groups V-VI and the technical feature linking all the groups (groups I-XV) is at issue.

Representative claims of group I:

Original Claim 1, a poly (ADP-ribose) polymerase (PARP) homolog which has an amino acid sequence which has a) a functional NAD<sup>+</sup> binding domain and b) no zinc finger sequence motif of general formula CX<sub>2</sub>CX<sub>m</sub>HX<sub>2</sub>C (SEQ ID NO: 30) in which m is an integral value from 28 or 30, and X radical are independently of one another, any amino acid; and the functional equivalents thereof.

Amended (01 March 2004) independent claim 1 representing group I:

An isolated and purified poly (ADP-ribose) polymerase (PARP) homolog selected from the group consisting of human PARP2 (SEQ ID NO: 2), human PARP3 type I (SEQ ID NO: 4), human PARP3 type 2 (SEQ ID NO: 6), murine PARP long form (SEQ ID NO: 8), murine PARP short form (SEQ ID NO: 10), and functional equivalents thereof which are at least 85 % homologous thereto, exhibit poly (ADP-ribose)-synthesizing activity, and have an amino acid sequence which a) a functional NAD<sup>+</sup> binding domain comprising the sequence motif PX(S/T)GX<sub>3</sub>GKGIYFA (SEQ ID NO: 11) and b) lacks zinc finger sequence motif of general formula CX<sub>2</sub>CX<sub>m</sub>HX<sub>2</sub>C (SEQ ID NO: 30) in which m is an integral value from 28 or 30, and X radical are independently of one another, any amino acid.

NOTE in both original claim 1 and amended claim 1, it is considered that the PARP homolog has an amino acid sequence which has a) NAD<sup>+</sup> binding domain and either lacks zinc finger sequence motif completely or lacks zinc finger sequence motif of general formula CX<sub>2</sub>CX<sub>m</sub>HX<sub>2</sub>C (SEQ ID NO: 30) in which m is an integral value from 28 or 30, and X radical are independently of one another, any amino acid.

Representative claims of group V:

Original Claim 6, a nucleic acid comprising, a) nucleic acid encoding the PARP homologs, complementary nucleotide sequences thereof, b) a nucleotide sequence which hybridizes with a sequence as specified in a); c) nucleotide sequence which are derived from the nucleotide sequences defined in a) and b) through the degeneracy of the genetic code.

Claim 7, nucleic acid of claim 6 comprising a) nucleotides of + 3 to +1715 shown in SEQ ID NO: 1; b) nucleotides +242 to +1843 shown in SEQ ID NO: 3; c) nucleotides +221 to +1843 shown in SEQ ID NO: 5; d) nucleotides +112 to +1710 shown in SEQ ID NO: 7; or e) nucleotides + to +1584 shown in SEQ ID NO: 9.

Representative claims of group VI:

Original claim 11, a transgenic mammal comprising a vector comprising the nucleotide sequence of claim 6.

It is noted that group VI depends upon and requires the nucleic acid of group V. Applicants are correct that groups V and VI share technical feature and thus groups V and VI are rejoined.

It is noted that both the independent original claim 1 and later amended claim 1, are drawn to a genus of polypeptides and not to a single species of protein, not to a single species of nucleic acid molecules encoding the PARP homolog of claim 1, as exemplified in Example 17. Accordingly, the unity of invention pursuant to Example 17 may not be applicable.

The polynucleotide of group V does not share a common structure or function or property with the polypeptide of group I. Further neither the nucleic acid molecule comprising a nucleic acid sequences of claim 11, nor the nucleotide sequence, which hybridizes with the sequence as specified in a) of claim 6, are required to or could possibly encode PARP homologs of claim 1, such that according to the PCT Administrative Instructions Example 17, the inventions would exhibit corresponding special technical feature.

Moreover, the polynucleotides of claim 6 (b) are not required to encode the PARP homolog (polypeptide) of group I. The nucleic acid sequences in claim 7; and claim 6, a) complementary nucleotide sequences, b) nucleotide sequences which hybridizes with sequences specified in a), c) nucleotide sequences which are derived from sequences of a), b), are non coding sequences of unspecified length, which may include mutations that disrupt the open reading frame.

Transcription and translation of non-coding strand would not result in the polypeptides of group I. Thus within the large number of polynucleotides encompassed by group V, many would not encode the polypeptides of group I. For these reasons Groups I and V lack corresponding technical features and the original Lack of Unity between groups I and V-VI was proper.

According to the PCT Rule 13.2, the special technical feature shall mean those technical features that define contribution which each of the claimed inventions, considered as whole makes over the prior art.

The technical feature of rejoined groups V and VI is considered as polynucleotide.

The technical feature of group I is considered as PARP homolog polypeptide.

The polynucleotide is made of nucleic acids, and the polypeptide is made of amino acids.

Thus, the polynucleotides of rejoined group V and the transgenic animal of group VI, and the polypeptides of group I are not linked by the same or corresponding technical feature as defined by PCT Rule 13.2.

The technical feature of groups II is antibody (a protein which is structurally, and functionally different from the protein of group I).

The technical feature of groups III is protein like compound (note it is not a protein).

The technical feature of groups IV is low-molecular weight effector (note it is not a protein).

The technical feature of groups VII is PARP deficient eukaryotic cell (absent of PARP).

The technical feature of groups VIII , IX, X, XI, XII, XIII , and XV is use of PARP homologs in different assays.

The technical feature of groups XIV is PARP protein or polynucleotides.

The technical feature of each group I, II, III, IV, VII and XIV is structurally different from each other.

Thus groups I, II, III, IV, VII and XIV are not linked by the same or corresponding technical feature as defined by PCT Rule 13.2.

Further the technical feature of group I is well known in the art, and does not contribute over the prior art, thus the unity of invention between the groups I-XV is lacking.

*It is noted that the special technical feature of the original claim 1 is the PARP homolog, having an amino acid sequence, which has a) a functional NAD<sup>+</sup> binding domain and b) no zinc finger sequence motif of general formula CX<sub>2</sub>CX<sub>m</sub>HX<sub>2</sub>C (SEQ ID NO: 30) in which m is an integral value from 28 or 30, and X radical are independently of one another, any amino acid; and the functional equivalents thereof.*

In the present instance neither the polynucleotide of group V and nor the polypeptides of group I (original claims) exhibit a corresponding special technical feature since a) Cherney et al (Proc. Natl. Acad. Sci. USA. Vol. 84 (1987), pages 8370-8374) teaches poly (ADP-ribose) polymerase (PARP) amino acid sequences which have homology to other DNA binding proteins. Cherney et al teach that the PARP proteins bind to DNA/NAD-binding proteins, and the presence of consensus nucleotide-binding site (residues 888-901) (pro-val-thr-gly-tyr-met-phe-gly-lys-gly-ile-tyr-phe-al), which refers to the NAD<sup>+</sup> binding domain of the instant invention (SEQ ID NO: 11); and lacks zinc finger motif of general formula CX<sub>2</sub>CX<sub>m</sub>HX<sub>2</sub>C (SEQ ID NO: 30) in which m is an integral value from 28 or 30 of the instant claim. Cherney et al teach the PARP has a zinc binding finger sequence of (residues 21-56) Cys-Xaa<sub>2</sub>-Cys-Xaa<sub>27</sub>-His-Xaa<sub>2</sub>-Cys, which is different from the zinc finger motif of general formula of instant claim. Thus, the PARP

taught by Cherney et al has a functional NAD<sup>+</sup> binding domain and lacks the zinc finger motif of general formula CX<sub>2</sub>CX<sub>m</sub>HX<sub>2</sub>C (SEQ ID NO: 30) in which m is an integral value from 28 or 30.

b) Lepiniec et al ( FEBS Letters, vol. 364, pages 103-108 (1995) (cited by the Examiner in the original Lack of Unity) teach *Arabidopsis thalina* cDNA homologue to animal poly (ADP-ribose) polymerase. The reference teaches that the APP (*Arabidopsis* PARP) has the PARP signature sequence 'tyr-gly-X-X-X-gly-lys-gly', which refers to the NAD<sup>+</sup> binding domain, and has no N-terminal zinc finger binding motifs of PARP.

In view of the teachings of both Cherney et al and Lepiniec et al, the original claim set lacks the technical feature linking the inventions. The technical feature of group I, the PARP homolog of original claim 1 is not considered as special technical feature in groups II-XV, because Cherney et al and Lepiniec et al teach the PARP homologs of group I. The technical feature linking groups I-XV does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art and hence the unity of invention is lacking.

With regard to newly presented 'an isolated and purified PARP homolog' of claim 1, it is noted that the polynucleotides of group V are not required to encode the PARP homologs and the functional variants thereof, of the amended claim 1. Further amended claim 1 recites a broad genus of amino acid sequences of SEQ ID NO: 2, 3, 4, 6, 8 and 10 and the functional variants thereof. An alignment of these sequences show that they have less than 36 % homology with the selected and examined SEQ ID NO: 2. See the attached Sequence Alignment. The sequences or the structure (NAD<sup>+</sup> binding domain and lack of zinc finger sequence of SEQ ID NO: 30) shared by SEQ ID Nos: 2, 3, 4, 5, 8 and the functional variants thereof, were taught by the prior art (see Cherney et al (1987) and Lepiniec et al (1995)).

According to PCT Rule 13.2, the PARP homolog of sequences of SEQ ID Nos: 2, 3, 4, 6, 8, and functional variants thereof, are not regarded as being of a similar nature because the common structure present (NAD<sup>+</sup> binding domain and lack of zinc finger sequence of SEQ ID NO: 30) is only a small portion of their structure (or sequence) (because the sequences share less than 36 % homology) and the commonly shared structure does not constitute a structurally distinctive portion. The homologs of SEQ ID Nos: 2, 3, 4, 6, 8, 10, and functional variants thereof, are not regarded as having same corresponding special technical features because the shared common structure is not a contribution over the prior art. See Cherney et al (Proc. Natl. Acad. Sci. USA. Vol. 84 (1987), pages 8370-8374) and Lepiniec et al ( FEBS Letters, vol. 364, pages 103-108 (1995). Both Cherney et al and Lepiniec et al teach PARP proteins which have NAD<sup>+</sup> binding domain, lack zinc finger motif of SEQ ID NO: 30. Thus, the shared common structure is not a contribution over the prior art, the inventions drawn to sequences of SEQ ID Nos: 2, 3, 4, 6, 8 and 10 lack unity.

## DECISION

Applicant's petition for reconsideration of Restriction requirement between groups I-XV under 37 CFR 1.144 is **GRANTED -IN-PART** for the reasons set forth above.

The lack of unity determination between groups V and VI has been withdrawn.

The lack of unity determination between groups I, II, III, IV, (rejoined groups V, VI), VII, VIII, IX, X, XI, XII, XIII, XIV and XV is maintained.

Any request for consideration must be filed within TWO (2) months of the mailing date of this decision.

The application will be forwarded to the examiner for preparation of an office action in response to the RCE filed on 01 March 2004.

Should there be any questions regarding this decision, please contact Special Program Examiner Julie Burke, by mail addressed to Director, Technology Center 1600, PO BOX 1450, ALEXANDRIA, VA 22313-1450, or by telephone at (571) 272-1600 or by Official Fax at 703-872-9306.



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